10/809,828

PTO 05-1168

CY=DE DATE=19880811 KIND=A1
PN=3 702 546

DISINFECTANT
[Desinfektionsmittel]

U. Jordan

UNITED STATES PATENT AND TRADEMARK OFFICE
Washington, D.C. December 2004

Translated by: FLS, Inc.

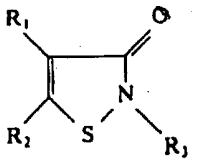
PUBLICATION COUNTRY	(10):	DE
DOCUMENT NUMBER	(11):	3702546
DOCUMENT KIND	(12):	A1
	(13):	Application
PUBLICATION DATE	(43):	19880811
PUBLICATION DATE	(45):	
APPLICATION NUMBER	(21):	P3702546.5
APPLICATION DATE	(22):	19870129
ADDITION TO	(61):	
INTERNATIONAL CLASSIFICATION	(51):	A01N 43/80
DOMESTIC CLASSIFICATION	(52):	
PRIORITY COUNTRY	(33):	
PRIORITY NUMBER	(31):	
PRIORITY DATE	(32):	
INVENTOR	(72):	Jordan, U.
APPLICANT	(71):	Jordan, U.
TITLE	(54):	DISINFECTANT
FOREIGN TITLE	[54A]:	Desinfektionsmittel

(57) /1*

A disinfectant for the medical sector is described, in particular for use in medical practices or hospitals, that comprises as the active substance isothiazoline-3-oxy and/or a derivative or derivatives thereof.

1. A disinfectant for the medical sector, in particular for use /2 in medical practices or hospitals, characterized in that it contains as the active substance isothiazoline-3-oxy and/or a derivative or derivatives thereof.

2. A disinfectant as recited in Claim 1, characterized in that the derivative of isothiazoline-3-oxy is of the general formula



where

R_1 is hydrogen or an alkyl group, in particular a methyl or ethyl group;

R_2 is hydrogen, halides, alkyl sulfates, aryl sulfonates, lineare or branched alkyl groups, in particular C_6-C_{12} alkyl groups and/or C_6-C_{12}-alkyl group mixtures; and

R_3 is hydrogen, alkyl groups, in particular a methyl group and/or linear or branched C_6-C_{12} alkyl groups and/or C_6-C_{12} alkyl group mixtures.

---

* Numbers in the margin indicate pagination in the foreign text.

3. A disinfectant as recited in Claim 2, characterized in that R_1 is hydrogen, R_2 halides, in particular chlorine and/or bromine, and R_3 is low alkyl groups, in particular a methyl group.

4. A disinfectant as recited in one of the Claims 2 or 3, characterized in that the active substance consists of a mixture of 5-chloro-2-methyl-4-isothiazoline-3-oxy and 2-methyl-4-isothiazoline-3-oxy.

5. A disinfectant as recited in Claim 2, characterized in that R_1 and R_2 are hydrogen and R_3 an alkyl group, in particular an n-octyl group.

6. A disinfectant as recited in one of the Claims 3 through 5, characterized in that the active substance is present in the form of a weak, dissociated complex of an inorganic salt, in particular an alkaline earth halide.

7. A disinfectant as recited in one of the previous Claims, characterized in that it contains the active substance at a concentration of 0.1 wt% to 0.0001 wt%.

8. A disinfectant as recited in Claim 7, characterized in that it contains the active substance at a concentration of 0.05 wt% to 0.01 wt%.

9. A disinfectant as recited in one of the previous Claims, characterized in that it is present in the form of a water-containing, liquid formulation, in which the active substance is dissolved, dispersed, and/or emulsified.

10. A disinfectant as recited in one of the Claims 1 through 8, characterized in that it is present in the form of a water-containing paste that, in addition to the active substance, also contains a cellulose-containing thickener.

11. A disinfectant as recited in one of the previous Claims, characterized in that, in addition to the active substance, it also has surfactants, in particular anionic and/or nonionic surfactants.

12. A disinfectant as recited in Claim 11, characterized in that it contains the surfactants at a concentration of 3 wt% to 60 wt%.

13. A disinfectant as recited in one of the previous Claims, characterized in that it has a pH of 4.5 to 10.5, in particular 6 to 7.5.

Description

The present invention relates to a disinfectant as recited in the precharacterizing part of Claim 1.

The known disinfectants used in the medical sector are aqueous solutions or emulsions of inorganic bleaching agents, such as hydrogen peroxide or sodium hypochlorite, or aliphatic or aromatic alcohols, such as phenols or phenol derivatives. These disinfectants generally contain the above-mentioned active substances at a concentration of approximately 10 wt% to approximately 15 wt% and are used undiluted or as approximately 10% aqueous solutions for antibacterial and/or antimicrobial treatment, for example of medical instruments, stock, premises, or hands.

Such known disinfectants, which contain as the active substances inorganic oxidation agents or phenols or phenol derivatives, frequently cause skin irritation or allergies or cause irritation of the mucous membrane. In some cases, in particular with phenol-containing or phenol derivative-containing disinfectants, the corresponding phenol or phenol derivative can enter the blood through the human skin, causing injury to internal organs, such as the liver. This occurs, in particular, if the disinfectant is used frequently and also contains the active substance at a high concentration. Moreover, such disinfectants do not kill all microorganisms. Thu, for example, it is known that certain viruses such as the TB bacillus are resistant to halogenated phenol derivatives.

The object of the present invention is to provide a /3 disinfectant of the type mentioned at the outset that, while providing a high biocidal effect on microorganisms found in the medical sector, is also easy on the skin.

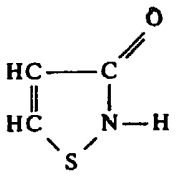
This object is achieved in accordance with this invention with a disinfectant that has the characteristic features of Claim 1.

The disinfectant of this invention, which may be used for disinfecting and/or cleaning, for example, equipment, instruments, stock, floors, and/or hands as well as linens and clothing in the medical sector, has as its active substance isothiazoline-3-oxy and/or a derivative or derivatives thereof.

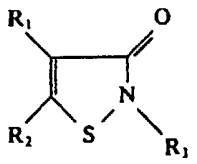
The disinfectant of this invention possesses a number of advantages. Thus, it has been found that the disinfectant of this invention is active against a great number of microorganisms, such as Alternaria dianthicola, Aspergillus niger, Aspergillus oryzae, Aspergillus repens Aureobasidium pullulans, Candida albicans, Chaetonium globosum, Cladosporium resinae, Lenzites lepideus, Lenzites trabea, Mucor rouxii, Penicillium funiculosum, Phoma glomerata, Phoma pigmentivora, Rhizopus stolonifer, Rhodotorula rubra, Saccharomyces cerevisiae, Trichophython interdigitale, Bazillus subtilis, Brevibacterium ammoniagenes, Staphylococcus aureus, Staphylococcus epidermidis, Enterobacter aerogenes, Escherichia coli, Proteus mirabilis Proteus vulgaris, Pseudomonas aeruginosa, and Salmonella typhosa. Algae, such as Ankistrodesmus falcatus, Chrorella pyronoidosa, Coccomyxa elongata, Scenedesmus obiquus, Nostoc sp., and Phormidium are killed or deactivated by the disinfectant of this invention to the extent that no growth occurs even 28 days after treatment with the agent. Moreover, even after long-term use of the agent of this invention no skin irritation, allergies, or irritation of the mucous membrane was found, so that it can be used even by people who are particularly sensitive. Due to the good biological degradability of isothiazoline-3-oxy and the corresponding derivatives, the disinfectant of this invention is particularly environmentally friendly. In addition, the disinfectant of this invention can be used with particular success to remove fatty

buildups, dirt particles, blood residue, etc., so that the disinfectant serves at the same time as a cleaning agent. This cleaning effect can be intensified by adding surfactants to the disinfectant of this invention, whereby anion-active or nonionic surfactants are preferably used. Moreover, an aqueous or water-containing solution or suspension or emulsion of the active substance does not foam or foams very little, so that such a disinfectant can also be used in disinfectant baths, in which there is a high degree of turbulance.

The disinfectant of this invention can contain as the active substance either isothiazoline-3-oxy alone, one or more derivatives thereof, or a mixture of isothiazoline-3-oxy with one or more derivatives of isothiazoline-3-oxy. The isothiazoline-3-oxy has the following chemical formula:

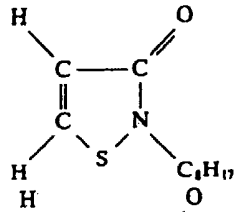


The derivatives of isothiazoline-3-oxy can be described by the following general chemical formula:

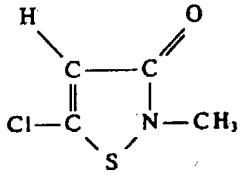


Here R_1 can be hydrogen or an alkyl group, in particular a methyl or ethyl group; R_2 hydrogen, halides, alkyl sulfates, aryl sulfonates, lineare or branched alkyl groups, in particular C_6-C_{12} alkyl groups and/or C_6-C_{12}-alkyl group mixtures; and R_3 hydrogen, alkyl groups, in particular a methyl group and/or linear or branched C_6-C_{12} alkyl groups and/or C_6-C_{12} alkyl group mixtures. It is also possible to use any desired combination of the above-mentioned groups as binding ligands R_1-R_3. The disinfectant of this invention preferably has as its active substance a derivative in which R_1 is hydrogen, R_2 a halogen, in particular chlorine and/or bromine, and R_3 a low alkyl group, in particular a methyl group.

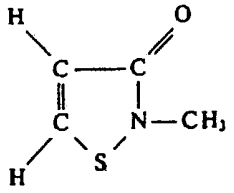
2-N-octyl-4-isothiazoline-3-oxy and/or a mixture of 5-chloro-2-methyl-4-isothiazoline-3-oxy and 2-methyl-4-isothiazoline-3-oxy can also be used as the active substance in the agent of this invention. These active substances possess an excellent biocidal effect, which is manifest in the rapid and complete disinfection or killing of the microorganisms listed above. Typically, the mixing ratio of 5-chloro-2-methyl-4-isothiazoline-3-oxy to 2-methyl-4-isothiazoline-3-oxy is approximately 2:1 to approximately 4:1, in particular 2.5:1 to 3:1. The compounds indicated above can be characterized by the following structural formulas:



2-n-octyl-4-isothiazoline-3-oxy



5-chloro-2-methyl-4-isothiazoline-3-oxy



2-methyl-4-isothiazoline-3-oxy

For particularly good stabilization of the 5-chloro-2- methyl-4-isothiazoline-3-oxy or 2-methyl-4-isothiazoline-3-oxy, these compounds can be present in the form of weak complexes of an inorganic salt, such as calcium or magnesium chloride. In this case, the complex dissociates in the aqueous system, so that a disinfectant of this kind has as its active substance the corresponding isothiazoline-3-oxy compound.

The concentration of active substance in the disinfectant of this invention depends on the intended use. Typically, such disinfectants that are used to disinfect or clean, for example, instruments, stock, or floors have a higher active substance concentration than disinfectants that are used to disinfect hands. Thus, it has been found that in a range of active substance concentrations between

approximately 0.1% and 0.0001%, the disinfectant possesses a good biocidal effect, i.e., the corresponding, above-mentioned microorganisms are sufficiently deactivated or killed. Particularly good results are achieved with active substance concentrations between approximately 0.05% and approximately 0.01%, since in this range of active substance concentrations no skin irritations occurred in albino rabbits in a closed patch test for 24 hours, regardless of the active substance that was used. Using the above-mentioned concentration range in human tests, even with repeated applications over a prolonged period of time no skin irritation or allergies could be determined, so that an active substance concentration range of approximately 0.05% to approximately 0.01% is particularly well suited for disinfecting hands, for example, or for objectes that come into contact with human skin. On the other hand, the concentration of active substance in disinfectants that are used for stock, floors, and the like can be correspondingly higher and preferably approximately between 0.1% and 0.05%.

Typically, the disinfectant of this invention is used in the form of a water-containing, liquid formulation. The active substance in this case, which comprises isothiazoline-3-oxy, one or more derivatives thereof, or a mixture of isothiazoline-3-oxy and one or more derivatives, is dissolved, emulsified, or dispered in a solvent, which may be, for example, water or a water-alcohol mixture. If isothiazoline-3-oxy, 2-n-octyl-4-isothiazoline-3-oxy, 5-chloro-2-

methyl-4-isothiazoline-3-oxy, or 2-methyl-4-isothiazoline-3-oxy is used as the active substance, then these active substances dissolve readily in water, the result being that a liquid disinfectant of this kind can be used without alcohol or alcohol mixtures as a solubilizer. Of course, on the other hand, it is also possible to add a suitable alcohol, such as isopropanol, so that a disinfectant of this kind will be better at dissolving fatty dirt. Moreover, a solvent mixture evaporates from water and isopropanol much more quickly, which has the advantage that hands, for example, disinfected with the substance will dry faster. Of course, it is also possible, on the other hand, to formulate the disinfectant of this invention such that it is in the form of a relatively viscous soap or solid disinfectant soap. For this purpose, a thickening agent such as, for example, methyl cellulose or ethyl cellulose in the proper concentration is added to the water-containing and/or alcohol-containing solution of the active substance.

If the disinfectant of this invention is to be used as a hand disinfectant, it may also contain oil restorative substances, such as aminoxide, proteins, or polyethylene glycols. Here, the concentration of such substances is typically approximately 0.3 wt% to approximately 2 wt%. It may also contain perfume additives in the usual concentrations, from ca. 0.05 to ca. 0.5 wt%.

If the disinfectant of this invention is also to contain stronger clearner, it may also have surfactants. Beside cationic surfactants, in particular anionic and/or nonionic surfactants may /5

be used whereby, depending on the field of application, they may be present in a disinfectant of this kind within a concentration range preferably of ca. 3% to ca. 60%. In addition, they may contain builders, such as those based on phosphates, borates, or inorganic or organic complexing agents, at a concentration of ca. 3% to ca. 15%. Moreover, the agent of this invention may have perfume additives at concentrations of ca. 0.05% to ca. 0.5%.

Since the optimum pH value of the disinfectant of this invention lies in a range of ca. pH 4.5 to ca. pH 10.5, a weak organic acid is also used to adjust the pH of the disinfectant, for example acetic acid, citric acid, uric cid, gluconic acid, aminosulfonic acid, isothionic acid, or sulfophthalic acid, where the quantity depends on the respective acid and the pH value that is to be produced.

In a particularly suitable form of administration for the disinfectant of this invention, the solution, dispersion, or emulsion of active substance or active substances described above, comprising the isothiazoline-3-oxy or derivative(s) thereof described above, is absorbed on a carrier material and/or absorbed by a carrier material. This results in a carrier material that is impregnated with the disinfectant and, optionally, cleaning active substance, which has sufficient moisture on its surface, so that it can be used directly for disinfecting and, optionally, cleaning. Possible carrier materials are materials with sufficient absorbency and wettable materials, such as felt, fleece, and paper or similar textile fabrics, such as felt,

fabric, or meshed materials. Typically, these carrier materials are charged with the solution, dispersion, or emulsion of active substance to between ca. 60% and ca. 160%, preferably between ca. 80% and 120%, with reference to the mass per unit surface of the respective carrier material, and then they are packed individually or multiply, so that evaporation or vaporization of the solvent(s) is prevented. This form of product is particularly easy to handle, since the carrier material, impregnated and wetted with the active substance and, optionally, with the above-mentioned additives (surfactants, builders, acid, perfume, restoratives) can be used immediately after removal from the package for disinfection and possibly cleaning, for example, work surfaces, stock, instruments, and the like.

Advantageous refinements of the disinfectant of this invention are found in the dependent claims.

The disinfectant of this invention will be explained below in greater detail with the help of exemplary embodiments.

Example 1

A cleaning concentrate was prepared using the following components:

1 wt%	2-N-octyl-4-isothiazoline-3-oxy
24 wt%	Isopropanol
26 wt%	anionic/nonionogenic surfactant mixture based on lauryl ether sulfate and ethoxilated alkyl phenols with a degree of oxethylation of 25
20 wt%	lauryl sulfate
29 wt%	water

Example 2

A second liquid disinfectant was prepared using the following components:

10 wt%	ethylene glycol
0.01 wt%	2-N-octyl-4-isothiazoline-3-oxy
0.033 wt%	lauryl alcohol ether sulfate
10 wt%	ethylene diamine tetraacetic acid
5 wt%	isopropanol
0.7 wt%	acetic acid
0.08 wt%	perfume additive
74.17 wt%	water

Example 3

A third disinfectant had the following composition:

10 wt%	ethylene glycol
0.04	wt% of a 14% water solution of 5-chloro-2-methyl-4-isothiazoline-3-oxy and 2-methyl-4-isothiazoline-3-oxy at a concentration ratio of 2.65:1
4.5 wt%	sodium-2-ethylhexyl sulfate, 40%
12.5 wt%	ethylene diamine tetraacetic acid
5 wt%	isopropanol
0.7 wt%	acetic acid
0.08 wt%	perfume
77.18 wt%	water

/6

Example 4

A fourth disinfectant was produced as follows:

10 wt%	polyethylene glycol MG 400
0.1 wt%	2-N-octyl-4-isothiazoline-3-oxy
4.5 wt%	of an anionic surfactant based on an ethylhexyl sulfate
12 wt%	ethylene diamine tetraacetic acid
5 wt%	isopropanol
0.7 wt%	acetic acid
0.06 wt%	citrus oil

67.62 wt% water

Example 5

A fifth disinfectant was prepared using the following components:

20 wt%	of an anionic/nonionogenic surfactant based on lauryl ether sulfate and ethoxilated alkyl phenols with a degree of oxethylation of 25
0.025 wt%	2-N-octyl-4-isothiazoline-3-oxy
2 wt%	fatty acid amide (as restorative)
2 wt%	alkyl ether sulfate
1 wt%	ethylene diamine tetraacetic acid
0.075 wt%	perfume
750 g	water

Disinfectant 5 is excellent as a liquid, disinfecting soap and, due to the addition of the restorative, it is particularly easy on the skin, so that it is suitable for long-term use.

Example 6

A universal cleaner, in particular, for example, for work surfaces, instruments, stock, etc., was prepared using the following substances:

2.7 wt%	of a lauryl ether sulfate
0.1 wt%	2-N-octyl-4-isothiazoline-3-oxy
0.1 wt%	ethoxilated fatty acid amide
0.1 wt%	ethylene diamine tetraacetic acid
0.05 wt%	perfume
96.95 wt%	water

Example 7

A skin cleanser was produced as follows:

60 wt%	alkyl sulfate
0.01 wt%	2-N-octyl-4-isothiazoline-3-oxy
3 wt%	1,2 propylene glycol
3 wt%	sodium chloride (as a thickener)
33.99 wt%	water

Example 8

A skin cleansing paste was prepared using the following components:

15 wt% alkyl sulfonate
0.025 wt% 2-N-octyl-4-isothiazoline-3-oxy
60 wt% of an ethoxilated methyl cellulose (2%, as a thickener)
0.05 wt% perfume
24.925 wt% water

Example 9

A skin cleansing agent was prepared using the following components:

10 wt% of a surfactant based on esters of higher fatty acids and fatty alcohols /7
0.125 wt% 2-N-octyl-4-isothiazoline-3-oxy
5 wt% glycerin
0.05 wt% perfume
84.93 wt% water

Example 10

A skin disinfectant, in particular for disinfection before surgery, was prepared from the following components:

15 wt% of an ethoxilated fatty alcohol
0.007 wt% 2-N-octyl-4-isothiazoline-3-oxy
15 wt% of a surfactant based on fatty alcohols
3 wt% of a restorative based on
2 wt% phosphoric acid 85%
5 wt% of a 10% iodine solution as additional disinfecting active substance
59.99 wt% water

Example 11

An eleventh disinfectant that is suitable, in particular, for veterinary purposes, had the following composition:

10 wt%	of a surfactant based on a polyether glycol
10 wt%	pine oil
0.04 wt%	of a mixture of 5-chloro-2-methyl-4-isothiazoline-3-oxy and 2-methyl-4-isothiazoline-3-oxy, Mischungsverhältnis 3:1
0.05 wt%	2-N-octyl-4-isothiazoline-3-oxy
20 wt%	of a surfactant based on
59.91 wt%	water

The disinfectants described above were tested quantitatively for their biocidal effect on microorganisms. For this purpose, a culture innoculated with Staphylococcus aureus (gram positive), Proteus vulgaris (gram negative), and Aspergillus niger (fungi), with a certain number of bacteria, was treated with the disinfectants described above. Before, one hour after, and 4 weeks after treatment with the disinfectants, the concentration of microorganisms was quantitatively determined by visual means. The results of the measurements are shown in the table below.

As seen in this table, after just an hour the bacteria or fungi have been almost completely killed. Even after 28 days no new bacterial or fungal growth could be found.

Desinfektionsmittel	Bakterien								
	Gram pos.			Gram neg.			Fungi		
	C_A	C_1	C_4	C_A	C_1	C_4	C_A	C_1	C_4
1	10^6	10	<10	10^7	10	<10	10^6	10	<10
2	10^7	10^3	10	10^8	10^2	10	10^6	10^3	10
3	10^6	10^2	10	10^7	10^2	10	10^6	10^2	10
4	10^6	10	<10	10^7	10	<10	10^7	10	<10
5	10^7	10^3	10^2	10^7	10^7	10	10^6	10^2	10
6	10^6	10	<10	10^8	10	<10	10^7	10	<10
7	10^7	10^3	10	10^6	10^2	10	10^6	10^3	10^2
8	10^6	10^2	10	10^7	10	10	10^6	10^2	10
9	10^6	10^2	10	10^8	10^2	10^2	10^7	10^2	10
10	10^6	10	<10	10^7	10	<10	10^7	10	<10
11	10^6	10	<10	10^6	10	<10	10^8	10	<10

[illegible] ohne Zusatz des Desinfektionsmittels; in Mikroorganismen pro ml

C4 = Initial concentration, i.e. without the addition of disinfectant, in microorganisms per ml.
C1 = 2 hours after disinfectant is added, in microorganisms per ml.
C4 = 4 weeks after disinfectant is added, storage at room temperature, in microorganisms per ml.

Key:

Disinfectant	Bacteria								
	Gram pos.			Gram neg.			Fungi		
	C_4	C_1	C_4	C_4	C_1	C_4	C_4	C_1	C_4
1 2									